alloantibody responses detectable within two weeks following either intravenous (n=2) or subcutaneous (n=2) injection of cells as well as following skin graft rejection.

These results suggest that exposure to donor cells following reduced intensity conditioning can result in robust immune modulation of antibody responses to allogeneic cells. B cell unresponsiveness is stable and does not depend on persistence of unresponsiveness at the T cell level or the persistence of donor cells. We speculate that this mechanism of immune modulation of B cell responses by allogeneic cells may play an important role in facilitating induction of transplantation tolerance through HCT.

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The MGH Miniature Swine as a Large Animal Model of HCT and Graft Versus Host Disease

Raimon Duran-Struuck [1,2], George F. Murphy [3], Roderick T. Bronson [4], David H. Sachs [1,2], Christene A. Huang [1,2], Thomas R. Spitzer [5,6]. [1] Transplantation Biology Research Center, Massachusetts General Hospital, Boston, MA; [2] Department of Surgery, Harvard Medical School, Boston, MA; [3] Department of Pathology, Brigham & Women's Hospital, Boston, MA; [4] Department of Microbiology and Immunobiology, Harvard Medical School, Boston, MA; [5] Bone Marrow Transplantation Unit, Massachusetts General Hospital, Boston, MA; [6] Department of Medicine, Harvard Medical School, Boston, MA

Graft-versus-host disease (GVHD) remains a frequent complication of hematopoietic cell transplantation (HCT) with skin being a principal target organ. Murine models have provided some insight into the mechanisms of this complex disease process. However, mouse skin differs from human skin, and results of studies in rodents may not translate well to the clinic. The pig is a well-recognized animal model for preclinical studies of skin including dermal toxicology, transdermal drug delivery and wound healing. Unlike skin of rodents, dogs or non-human primates, porcine skin is similar to human skin in terms of structure of epidermal rete ridges, hair follicle structure and density, and presence of sweat glands and subcutaneous fat. Because of the similarities of pig skin to human skin and availability of swine with defined MHC genes, MGH miniature swine provide a valuable pre-clinical model of HCT for studies of graft-versus-host disease. HCT between MHC matched or mismatched animals can be performed to mimic clinical HCT scenarios with outcomes that closely resemble those observed in human HCT recipients. With myeloablative conditioning, HCT across MHC barriers is most often fatal, with animals developing severe grade III-IV GVHD involving the gastrointestinal tract (GI), liver and skin. We have developed a comprehensive GVHD scoring system for pigs which parallels that used clinically (see chart). Unlike rodent models, miniature swine provide an opportunity to perform extended longitudinal studies, since multiple tissue biopsies can be taken without the need to sacrifice the animal. Given the similarities of GVHD in pigs and humans, we hope that the utilization of the pig and scoring system facilitates scientific discourse between the laboratory and the clinic. We anticipate that results of swine studies will be applicable to the development of new strategies to improve GVHD identification and treatment in clinical HCT scenarios.

TBRC SWINE CLINICAL GVHD ASSESSMENT R Duran 2010

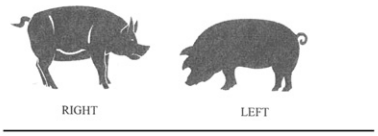
Date Of Assessment:
Transplant Day:

STAGE						
	0	1	2	3	4	
Skin	☐	☐	☐	☐	☐	% body rash:
Upper GI	☐	☐				
Lower GI	☐	☐	☐	☐	☐	Volume stool: Color stool
Liver	☐	☐	☐	☐	☐	

SKIN (draw below)	UPPER GI	LOWER GI
0 = No rash 1 = Maculopapular rash on < 25% of BSA 2 = Maculopapular rash on 25% to 50% 3= Rash > 50%, generalized erythroderma 4 = Stage 3 plus bullae and desquamation	0 = No nausea and vomiting 1 = Persistent nausea, vomiting or anorexia	0 = no diarrhea 1 = soft stools 2 = diarrhea 3 = bloody diarrhea 4= b diarrh+hunched

LIVER (max total=4)

Bilirubin	ALKP	ALT	AST
0 = < 0.8 mg/dl	0=<294	0= <43	0=<65
0.25 = 0.8 – 1.5 mg/dl	0.25=294-500	0.25=43-90	0.25=65-130
0.5 = 1.5 – 3 mg/dl	0.5=500-1500	0.50.0=90-180	0.50=130-500
0.75 = 3 – 9 mg/dl	0.75=1500-3000	0.75=180-400	0.75=500-1500
1= > 9.0mg/dl	1.0=>3000	1.0=>400	1=>1500



Overall Grading of Acute GVHD

	$_0$☐ Grade 0	$_A$☐ Grade 1	$_B$☐ Grade 2	$_C$☐ Grade 3	$_D$☐ Grade 4
SKIN	0	1	2	3	4
LOWER GI	0	0	1-2	3	4
UPPER GI	0	0	1		
LIVER	0	0	1-2	3	4

Note: Subscripts relate to grading at MGH clinic

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Long-Term Follow up of SAA Patients Allografted with a Non-ATG-Based Conditioning Regimen, Using Pbscs as the Sole Source of Engraftment: A Single Center Experience of 53 Patients Above the Age of 20 Years

Omar A. Fahmy Sr.. Bone Marrow Transplantation Unit, Nasser institute for research and treatment, Cairo, Egypt

Background: Allogeneic HSCT from an HLA-matched sibling donor is the recommended treatment approach in patients with SAA, at least up to the age of 40 years. Cyclophosphamide (Cy)-ATG is the standard, non-myeloablative conditioning regimen, while BM stem cells are the preferred source of engraftment.

Aims: We have already published our data regarding the use of PBSCs in patients with SAA conditioned with the Fludarabine (Flu)-Cy regimen (EBMT, Czech Republic 2005, Poster Abst # 782 / CBMTG, Montreal 2008, oral Abst # 02). In this single arm prospective study, we investigated the use of Flu–Cy to allograft SAA patients >20 years old, using PBSCs.

Patients & methods: In the time period between May 2003 and December 2009, 53 heavily pre-transfused SAA patients received allogeneic HLA- identical sibling PBSCs at the BMT unit of Nasser institute, Cairo, Egypt. All patients were above the age of 20 years (range 21- 41 years, mean 27 years). The regimen consisted of Flu at a total dose ranging from 75mg-120mg/ m2, and a total Cy dose of 200mg/kg. Our primary endpoints were incidence and severity of chronic GVHD, as well as DFS & OS. Cyclosporine & Methotrexate were used for GVHD prophylaxis.